COMMUNICATIONS:

4. CASE SERIES: SUB-FERTILITY AND MILD HYPOTHYROIDISM

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ABSTRACT

Mild degree of hypothyroidism may be associated with reduced fertility as depicted by two cases reported below.

CASE 1

A lady of age 23 years came with the complain of obesity, had a technetium thyroid scan on 8 July 2001 which revealed mild degree of hypothyroidism. She had a past history of ovarian cyst, which was operated on 19 years of age. She started thyroxine 50 micrograms (mcg) per day and checked her T^3, T^4, & TSH levels at few-monthly intervals (Table-1), but she had two abortions in Dec.'02 & May '03 likely due to inadequate and irregular thyroxine ingestion, e.g., sometimes she takes 25 mcg/ day.

CASE 2

A lady of age 30 years came to CNMU Rangpur with the complaints of anorexia, constipation, cold intolerance, voice changes, irregular menstruation and secondary infertility. Her only child is a daughter of 6 years. Her past history includes thyroidectomy for multinodular goitre in May 1999 followed by inadequate supplementation therapy-she is taking only 50 micrograms of thyroxine daily. She had only one thyrotropin (TSH, thyroid stimulating hormone) estimation elsewhere in 2001 which was 1.11 μU/ml (normal range: 0.23-4), and as it was normal, no estimations of thyroid hormones (T_3 & T_4) were done there. We have done her thyroid function tests (Table 2) and found her to be mildly hypothyroid and advised to increase her daily thyroxine dose to 100 micrograms.

Table 1 Hormones levels of Case 1

22 Oct. 03	May 03	Oct.02	11 Aug. 02	17-01-02
T_3 = 0.23	2.4	2.15	4.1	2.8
T_4 = 108	152	108	243	142
TSH=2.85	8.21	5.75	8.58	13.5

Normal ranges: T_3 = 0.8 – 3.16 nmol/L T4 = 64-175 nmol/L TSH= 0.4-5 mIU/L

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Table 2 Thyroid function tests of case 2

Date	Test	Values
7 July 2003	Radiommuno assay (RIA)	T_3 = 0.2 nmol/L T_4 = 106 ,, TSH = 2 mIU/L
10 Sept. 2003 Radioiodine uptake test		Normal ranges
2 hours uptake	3.5%	(5 – 15%)
24 hours uptake	22.3%	(16 - 40%)

DISCUSSIONS

The introduction of radioimmunoassay (RIA) by Yalow and Berson in 1959 provided superior measures for serum T_3, T_4 and TSH.[1] Clinical features of hypothyroidism depend on the duration and severity of the condition. A consequence of prolonged hypothyroidism is the infiltration of many body tissues by the mucopolysaccharides, hyaluronic acid and chondroitin sulphate, resulting in a low-pitched hoarse voice, poor hearing, slurred speech due to a large tongue and compression of the median nerve at the wrist,[2] menorrhagia, amenorrhea, infertility, galactorrhea, impotence, cold intolerance, constipation, goitre, tiredness and somnolence. T_3 concentrations may not discriminate reliably between euthyroid and hypothyroid patients, but in our case 1 it was the only hormone, which was low. Subclinical hypothyroidism is most often encountered after radioiodine (I-131) therapy or thyroidectomy and may persist for many years. With pituitary hypothyroidism, since serum TSH is not elevated, serum T_4 estimations are used to monitor the dose of thyroid replacement, which is increased until the serum T_4 concentration is within the upper normal range.[3,4] The subtle presence of hypothyroidism, which may be associated with elevated prolactin levels, demands screening of anovulatory and amenorrheic women with a TSH level,[5] although it seems rather extravagant to measure TSH in such a large number of patients for such a small return, because treatment for hypothyroidism is so simple and is rewarded by such a prompt return of ovulatory cycles, and, if galactorrhea is present, by a disappearance of the breast secretions (a slower process that can take several months). Effect of thyrotoxicosis and its treatment by methimazole and radioiodine (I-131) on gonads is well-evidenced,[6-7] however, that of mild hypothyroidism seems yet to be elucidated fully. Thyroid hormones are essential for mammalian life as they regulate many key biochemical reaction, especially protein synthesis and enzymatic activity. They also play a determining role in the process of early growth and development of fetal and first 2-3 years of postnatal life.[8] Brain damage to the developing child is entirely preventable by correction of iodine deficiency of the mother. During pregnancy and estrogen therapy, the need for thyroxine is increased.[9] Screening of neonates for congenital hypothyroidism is being done in many countries,[10] but screening of pregnant woman for hypothyroidism is not yet universal.[11] Haddow et al. and Utiger encouraged adequate iodine intake and it should be increased during pregnancy.[12,13] When the iodine supply to the thyroid gland is limited, the gland produces relatively more T_3 than T_4. When T_4 levels are low, target tissues also convert T_4 to T_3 However, the brain can only take up T_4 but not T_3, so brain function is affected when T_4 levels are low even though there may be sufficient T_4 and T_3 to carry out the function of thyroid hormones in other organs/ tissues. This is particularly important for the fetus in the first half of pregnancy. If maternal T_4 levels are low, the

fetal brain will be exposed to low T_4 levels, and this will result in brain damage.[14]

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